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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/571,199   | 03/09/2006  | Hiroshi Nakajima     | NAKAJIMA 7          | 3687             |
| 1444   | 7590        | 03/25/2010           | EXAMINER            |                  |
| BROWDY AND NEIMARK, P.L.L.C.<br>624 NINTH STREET, NW<br>SUITE 300<br>WASHINGTON, DC 20001-5303 |             |                      |                     | CHONG, YONG SOO  |
| 1627   |             | ART UNIT             |                     | PAPER NUMBER     |
| 03/25/2010   |             | MAIL DATE            |                     | DELIVERY MODE    |
|  |             |                      |                     | PAPER            |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |
|------------------------------|------------------------|---------------------|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                              | 10/571,199             | NAKAJIMA ET AL.     |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |
|                              | Yong S. Chong          | 1627                |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 03 March 2010.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 43,44 and 46-51 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 43,44 and 46-51 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

|  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/9/09</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application |
|  | 6) <input type="checkbox"/> Other: _____ .                        |

## DETAILED ACTION

### ***Status of the Application***

This Office Action is in response to applicant's arguments filed on 12/23/09 and 3/3/10. Claim(s) 1-42, 45 have been cancelled. Claim(s) 48-51 have been added. Claim(s) 43-44, 46-51 are pending. Claim(s) 43-44 have been amended. Claim(s) 43-44, 46-51 are examined herein.

Applicant's amendments have rendered all rejections of the last Office Action moot, therefore hereby withdrawn. The following new rejections will now apply.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 43, 48, 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a

question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 43 recites the broad recitation "a benzylisoquinoline derivative of formula I with the proviso that it is not neferine, liensinine, or isoliensinine", and dependent claims 48 and 51 recites "a benzylisoquinoline derivative of formula I" which is the narrower statement of the range/limitation.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 43-44, 46-51 are rejected under 35 U.S.C. 103(a) as being obvious over Rafferty et al. (US Patent 4,719,234) in view of Yasukawa et al. ("Inhibitory Effect of Cepharanthine and its Related Compounds on 12-O-Tetradecanoylphorbol-13-acetate-induced Inflammation and Inhibition of Tumor Promotion by Cepharanthine in Two-Stage Carcinogenesis in Mice" Nihon Univ. J. Med. 31, 229-234, 1989, of record).

The instant claims are directed to a method of treating pain comprising administering a compound of formula I.

Rafferty et al. teach compounds with anti-inflammatory activity for the treatment of neuralgia, dental pain, headache, and migraine (col. 1, lines 10-18). The anti-inflammatory agents of the present invention may be formulated into pharmaceutically acceptable dosage forms by conventional methods known to the pharmaceutical art. In general, a preferred method of administration is by oral dosage forms, such as tablets, capsules, pills, powders or granules (col. 4, lines 1-9).

Examiner notes that it would be obvious to one of ordinary skill in the art to administer the composition taught by Rafferty et al. in an oral dosage form, such as with water, food, or other health food, beverage, or drinkable preparation.

However, Rafferty et al. fail to disclose a compound of formula I.

Yasukawa et al. teach that cepharanthine and its related compounds possess anti-inflammatory properties and thus are useful in treating tumors in mice (abstract). A preferred anti-inflammatory agent is armepavine (figure 2 and table 1).

Therefore, it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to substitute the anti-inflammatory

agent, armepavine, as taught by Yasukawa et al., for the anti-inflammatory agent in the method of treating pain, as taught by Rafferty et al.

A person of ordinary skill in the art would have been motivated to substitute the anti-inflammatory agent, armepavine, as taught by Yasukawa et al., for the anti-inflammatory agent in the method of treating pain, as taught by Rafferty et al. because of the functional equivalency of both compounds possessing anti-inflammatory properties. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating pain by administering armepavine.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/  
Primary Examiner, Art Unit 1627

YSC